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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/391,861	09/07/99	THOMASON	A 99.371

020306 HM22/0926
MCDONNELL BOEHNEN HULBERT & BERGHOFF
300 SOUTH WACKER DRIVE
SUITE 3200
CHICAGO IL 60606

EXAMINER	
NGUYEN, D	
ART UNIT	**PAPER NUMBER**
1633	17

DATE MAILED: 09/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/391,861	Applicant(s) THOMASON ET AL.	
	Examiner Dave Nguyen	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-13 and 36-46* is/are pending in the application.

4a) Of the above claim(s) *37,38,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-13,36 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13, 16
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

This application has been assigned to a new examiner since the previous examiner has left the Office.

The specification has been amended, claims 1, 2, 12, 13, 36, 39 and 40 have been amended, claims 44-46 have been added, and claims 6 and 14-35 have been canceled by the amendment filed July 5, 2001.

Claims 44-45 are directed to subject matter not drawn to the claimed invention as recited in the elected and originally filed claims, and thus, will not be examined in this application. The subject matter as claimed in claims 44 and 45 are directed to *in vitro* and/or *in vivo* assays for identifying candidate compounds for inhibiting FGF-like polypeptide or FGF-like production, readable on class 435, subclasses 6 and 7.1, which method were not claimed in the originally elected claims.

This application contains claims 37, 38, 44 and 45 drawn to an invention non-elected with traverse as indicated in previous and this office action. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) MPEP 821.01. Claims 37, 38, 44 and 45 remain withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as being drawn to a non-elected invention.

Claims 1-5, 7-13, 36, 39-43 remain and claim 46 is rejected under 35 USC 112, first paragraph, for the reasons as set forth on pages 2 and 3 of the Office action dated January 4, 2001.

Applicant's response (file July 5, 2001) has been considered by the examiner but is not found persuasive for the reasons set forth in the stated rejection and for the following reasons:

In response to applicant's assertion (the response, pages 7 and 8) that a BLAST search shown in Exhibit A indicates that nearly all the sequences using SEQ ID NO: 2 in a BLAST search were found to be members of the FGF family of proteins, and that instantly-claimed human FGF-like polypeptide is mostly closely related, but not identical, to an FGF (FGF-21) that is most preferentially expressed in the liver, as

shown in Exhibit B, the comments are not found persuasive because none of the of the information or description shown in Exhibit A or B is provided by the as-filed specification at the time the invention was made. The as-filed specification does not provide any information or written support to show a well-established, or a specific and substantially credible utility for the subject matter being sought in the presently pending claims, particularly since it is well-recognized in the art that FGFs are members of a protein family which has demonstrated a broad range of biological activities involving cell growth and differentiation such as angiogenesis, morphogenesis, and wound healing. Neither the as-filed specification nor Exhibit A nor Exhibit B provides any factual evidence to indicate that as the as-filed specification provides a well-established, or a specific and substantially credible utility for the subject matter being sought in the presently pending claims.

In response to applicant's assertion (the response, page 8) that since the specification on page 5, lines 3-14 contemplates that the FGF-like molecules is secreted into the bloodstream where it may exert effects on distal sites, and that the claimed FGF-like molecules then may have a specific utility for stimulating cells within or near the liver, regulating intestinal cell activity, or stimulating pancreatic beta islet cells, the comments are not found persuasive because the fact that the as-filed specification contemplates that the claimed FGF-like molecules regulates growth and differentiation of cells within the liver and of other cell types after secretion from the liver, does not provide any credible support for a well-established, or a specific and substantially credible utility for the subject matter being sought in the presently pending claims. What is exactly the specific biological function of SEQ ID NO: 2 in growth, differentiation of cells in liver or of any other cell types on the basis of applicant's disclosure. In light of the fact that the FGF family of FGF proteins is enormous and involves a number of specific biological functions but distinct in growth and differentiation, one skilled in the art would not have recognized that the as-filed specification has provided any specific and substantial utility for the subject matter being sought in the presently pending claims. The specification as a whole clearly generalizes and merely speculates a number of potential utilities, some of which are not even related and are distinct and contrary to one another, *e.g.*, stimulating pancreatic beta islet cells, stimulating cells within or near the liver, regulating intestinal cell activity as opposed to the making

of transgenic mice expressing any claimed FGF-like transgene that exhibit an abnormal phenotype generally characterized as inhibited or delayed maturation, which includes reduced body weight, reduced liver weight as percent of body weight (page 4 of the specification and also asserted as a specific and substantially credible utility on page 8 of the response), stimulation of angiogenesis, and yet also inhibition of angiogenesis, therapeutics in treatment of diabetes and yet also therapeutics in stiulation of corneal epithelium, lens, or retinal tissues, and yet also treatment of neuronal and/or hematopoietic cells (page 5 of the specification). These possible utilities-other than as a possible object of scientific inquiry-was not yet established by the as-filed specification at the time the invention was made.

A simple statement in the as-filed specification as to the similarity between the structure applicant's claimed FGF-like polypeptide and well-established FGF of the prior art, *e.g.,* 32% identify to FGF-6 and 28% identity to FGF-4 for SEQ ID ID NO: 3, or even less in identity for SEQ ID NO: 1, since SEQ ID NO: 3 was used to isolate SEQ ID NO: 1, which sequences (SEQ ID NO: 1 and 3) only share 76% in identity, which is the only main basis or nexus for applicant's claim of merely speculative or potential utiltity which does not have a real world value and does not provide a **currently available specific benefit to the relevant public** does not meet the requirements of 35 USC 101.

Furthermore, all of the asserted utilities as indicated in the as-filed specification (pages 4 and 5) amounts to only generalized and non-specific utilities, wherein each of the asserted utilities requires additional knowledge about the **specifically biological function of any FGF-like transgene as encompassed by the genus claimed invention transgene as encompassed by the genus claimed invention**, whether there are specific ligands and/or well-established biological pathway responsible for any of applicant's asserted utilities linked to applicant's claimed FGF like transgene, *e.g.,* if so, **their identity**. As a result, since each of applicant's asserted utilities requires additional knowledge about any of applicant's claimed FGF-like transgene before any of applicant's claimed FGF like-transgene can be used for a specific purpose or before a real word benefit exists in currently available form, the utility requirement has not been met, *e.g.,* where applicant's asserted utilities constitute research on the claimed product itself, there is not apparent *immediate* benefit to the public that the patent system is designed to protect.

In view of the reasons set forth in the stated rejection and in view of the reasons set forth in the preceding paragraphs, applicant's assertion and comments on pages 7 and 8 of the response are not found persuasive. Thus, a skilled artisan would not have recognized that, **at the time the invention was made,** this as-filed specification provides any credible support for a well-established, or a specific and substantially credible utility for the subject matter being sought in the presently pending claims.

Claims 39 and 40 remain rejected under rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth in pages 4 and 5 of the office action dated January 4, 2001.

In response to applicant' s assertion (the response, page 9) that by a simple disclosure of transgenic mice expressing an FGF-like transgene exhibiting an abnormal phenotype, of contemplation of localization and/or effect of the FGF-llike mRNA expression in the liver, applicants has met the written description requirement for claiming a genus of nucleotide sequences encoding a polypeptide that is at least 80% identical SEQ ID NO: 2 or 4; of allelic and splice variants of SEQ ID NO: 1 or 3, or the unspecified ATCC; of nucleotide sequences encoding polypeptide fragments of at least 25 amino acid residues with the activity of the polypeptide of SEQ ID NO: 2 or 4 or able to generate unspecified antibodies; of nucleotide sequences which hybridizes to and exhibits the activity of or is complementary to any of the above stated nucleic acid sequences; and of genus of mutant nucleotide sequences of SEQ ID NO: 2 or 4 with at least one conservative amino acid substitution, insertion, deletion, C-terminal and/or N-terminal truncation, the comments are not found persuasive because of the reasons set forth in the stated rejection. Note that an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or assays and/or formula containing unspecified molecular structures of FGF like polypeptide encoded nucleotide sequences that are essential for the making the genuses of unspecified material(s) as claimed; what is required is the knowledge in the

prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of each of the genus(es) that must exhibit the disclosed biological functions as contemplated by the as-filed specification.

It is not sufficient to support the present claimed invention directed to numerous number of genuses of nucleotide sequence(s) as claimed in claims 1(d) - 1(e), 39(a) - 39 (f), 40 (a) to 40 (h), for example, with no chemical structure, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any and/or all other material(s) of nucleotide sequene(s) of FGF-like transgene having any of the biological functions as contemplated by the specification and the claims. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Claiming unspecified molecular structures of gene(s) that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of the claimed FGF-like transgenes that must exhibit any of the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-5, 7-13, 36, 39-43 remain, and claim 46 is rejected under 35 U.S.C. 112, first paragraph,

as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly in view of the reasons set forth on pages 6-8 of the office action dated January 4, 2001, excluding paragraphs indicating the deposit rule requirement.

In response to applicant' s assertion (the response, page 10) that one skilled in the art would know how to make and use and practice any of the subject matter now being sought in the claims, that US Pat No. 5,217,880 provides the factual evidence for a skilled artisan to practice the claimed invention in the context of therapeutic applications, the comments are not found persuasive for the reasons set forth in the stated rejection, particularly since applicant's comments are conclusory, and express an opinion without any factual evidence to overcome the art-recognized limitations and reasons as set forth in the stated rejection. Furthermore, a simple assay for determining a potential antisense inhibitor provided by the prior art, as exemplified the '889 patent, is not the same as an antisense gene therapy method of regulating or modulating levels of any FGF-like polypeptide at any target cell or tissue of any animal by using any antisense molecule encompassed by the method cited in claim 36 or 46, particularly given the reasons set forth in the stated rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9, 12, 13, 36 and 40 remain and claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, particularly in view of the reasons set forth on page 9 of the Office action dated 1/4/2001.

Claim 39 remain indefinite in the recitation of a Markush group which recites undue multiplicity, *e.g.,* (a)...;(b)...or (a) wherein the polypeptide has an activity of the polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4; (c)....; (a) ; or (b); (d)...; or (a) – (c), that renders the claim vague and indefinite.

In response to applicant' s assertion (the response, page 10) that since a skilled artisan could readily generate fragments of the claimed sequences of claim 39(a) that lack "an activity of the polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4," the use of this phrase in claim 39(c) is not redundant, the comments are not found persuasive because the entire claim when read as a whole does recite an improper Markush group which recites identical element (a), (b), (c) in multiple times and contains multiple dependent elements that render the claim being vague and indefinite as to applicant's intended scope of the claim in its entirety. The fact that a skilled artisan could readily generate fragments of the claimed sequences of claim 39(a) that lack an activity of the polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 4 does not negate the fact that applicant's Markush group in claim 39 is an improper Markush group that render the claim indefinite. Furthermore and on the contrary to applicant's comments, the phrase cited in claim 39(c), *e.g.,* (c).....; (a); or (b); encoding a polypeptide...., remains unclear is its meaning and does not reflect the further and definite limitation as asserted by applicants in the response. It is not apparent as to what is exactly meant by the phrase when the claim is read in its entirety.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Kimberly Davis, whose telephone number is **(703) 305-3015**.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Clark*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1633

DAVE T. NGUYEN
PRIMARY EXAMINER